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FINAL REPORT

United States Air Force

CONFERENCE GRANT: FASEB Summer Research Conference on
Retinal Neurobiology and Visual Processing

GRANT NUMBER: F49620-96-1-0128

PERFORMANCE PERIOD: 5/01/96 through 4/30/97

GRANT AMOUNT: \$7,500

PRINCIPAL INVESTIGATOR: David Copenhagen

GRANTEE INSTITUTION: Federation of American Societies for Experimental Biology
9650 Rockville Pike
Bethesda, MD 20814-3998

DATE OF REPORT: October 3, 1996

FASEB Summer Conference
July 13-18, 1996
Saxtons River

RETINAL NEUROBIOLOGY AND VISUAL PROCESSING

This meeting was the third Summer Conference focused on the retina. There were 30 invited speakers who were divided about evenly into 9 sessions. The participants were a good mix of younger and more established scientists from within US. and abroad. Age-wise most of the participants fell evenly into groups of 30, 40 and 50 year-olds. Discipline-wise, we drew participants from areas in molecular biology through computational neuroscience.

The sessions were organized as follows: 1) Visual Performance, 2) Signal Transduction and Modulation in ON Bipolar cells, 3) Mechanisms and Functions of Gap Junction Coupling, 4) Ionic Channels to Machines, 5) Synaptic Mechanisms in the Outer Plexiform Layer, 6) "Potpourri" (Speakers selected from those who submitted poster abstracts), 7) GABA_C Receptors, 8) Synaptic Processes in the Inner Plexiform Layer and 9) Ecology of Vision. The first session highlighted how the retina sculpts and limits visual performance. A particularly striking talk by Tom Reuter tied the visual performance of prey catching in toads to the "noise" generated in rods of this animal. The session on ON Bipolar cells included a talk by Duvoisin who was attempting to clone the elusive cGMP-gated channel in these neurons and a paper by Laura Frishman who was able for the first time to dissect the signal generated by ON bipolar when recording from anesthetized cats. This technique promises to be useful to diagnose visual function in human subjects. In the gap junction coupling sessions the talks were highlighted by work of Massey and Mills who are beginning to dissect the differences in various retinal gap junction complexes by observing the differential flow of different-sized dye molecules between coupled cells. The session on ionic channels flowed seamlessly from discussion of specific ion channels in different fly eyes to a video-taped presentation of a robot whose visual behavior was based on the circuitry of the fly's visual system. In the synaptic mechanisms session, the topics ranged from the regulatory processes that might control the release of glutamate from rods and cones to how the glutamate actually diffuses to the postsynaptic cells to the neuromodulatory actions of glutamate. It is clear that the speakers are working in an intensely-studied and very productive area that promises to be an exemplary system to understand glutamatergic synaptic transmission.

In order to provide opportunities for "hot, new" topics, we devoted one session to platform presentations from poster submissions. All of the talks were well received. The topics ranged from an examination of the calcium currents in mouse bipolar cells to the waves of calcium that course through neonatal retinas during development to a new behavioral test for zebrafish vision. A new receptor for the inhibitory neurotransmitter GABA was discovered recently. This receptor is known to control synaptic transmission from bipolar cells to ganglion cells. Our session on these GABA_C receptors showed that much progress has been made in understanding the functioning of these receptors at the molecular level. For the session on synaptic processing in the inner plexiform layer the speakers presented striking new findings on how

neurotransmitter might be released and on how desensitization of postsynaptic receptors plays a vital role in determining the time course of a light response. In the last session we moved to a survey of ecological and evolutionary issues of visual processing. The talks were highlighted by a presentation of how fish cones are evolved to respond to polarized light. Two speakers discussed their work in a rapidly expanding field that addresses how the retina is "constructed" to optimize the transmission of the visual field representation to the brain with optimal fidelity.

The response to this conference was very enthusiastic. Thirteen of 59 participants who completed evaluation forms ranked the meeting as the best conference they had attended. 41 of 59 ranked it as being in the top 10%. The attendance has grown steadily since the first conference on retina was held in 1992.

In addition to the paper sessions we organized two workshops on subsequent afternoons. These were very well attended and allowed much open discussion of technical and theoretical approaches to studying retinal neurobiology and visual processing. The workshops were prearranged so speakers arrived knowing they would be giving a short informal talk.

We were able to secure funding from the National Science Foundation, Office of Naval Research and the Air Force Office of Research. In addition three instrument companies donated funds.

Every effort was made to facilitate the participation of younger scientists. One of the "rules" we established was that no speaker was invited who talked at the 1994 meeting. We wanted to ensure that more scientists and more laboratories had a chance to present their work. I think this policy helped keep the meeting fresh and interesting. We did ask some of the older, established scientists to chair the sessions and give a 10 minute overview/introduction for the topic. These introductions were very helpful in bringing the graduate students up to speed.

At the business meeting, we unanimously decided to schedule another meeting for 1998 in Saxtons River. The chair of the 1998 meeting will be:

Markus Meister
Department of Cellular and Molecular Biology
Harvard University
16 Divinity Ave.
Cambridge, MA 02138
Tel: (617) 496-8301, Fax (617) 495-9300

Sincerely,

A handwritten signature in cursive script, reading "David Copenhagen". The signature is fluid and stylized, with a long horizontal flourish extending from the end.

David Copenhagen
Chair, 1996 Summer Conference on
Retinal Neurobiology and Visual
Processing

Schedule of Scientific Sessions and Workshops
 (As of June 27, 1996)
 (Subject to minor modifications)

14 July

Visual Performance

Moderator: Peter Sterling

8:40-9:00 am Welcome etc.

9:00 Introduction

9:10 am Marty Banks (Title?)

9:55 am Stelios Smirnakis "Retinal processing adapts dynamically to second order image statistics."

10:40 am Coffee Break

11:00 am Tom Reuter "When does the random distribution of discrete photoreceptor events limit the sensitivity of the visual system?"

11:45 am* David Brainard "Behavioral consequences of retinal sampling: interactions between space and color"

2:00-4:00 PM Workshop: Computational Approaches to Retinal Research

Moderator: Udi Kaplan

- 1) Norberto Grzywacz "A model of directional selectivity: the melee among GABA, acetylcholine, and glutamate."
- 2) Buster Boahen "The role of spatio-temporal highpass filtering in the inner vertebrate retina: A computational approach."
- 3) William Beaudot "Adaptive and spatiotemporal dynamics in the vertebrate retina: A 'structure to function' approach."
- 4) Frank Werblin "Computational prediction and experimental verification of a new form of edge-enhancement (without lateral inhibition) in retina."

Signal Transduction and Modulation in On Bipolar Cells

Moderator: David Copenhagen

7:30 pm Introduction

7:40 pm Robert Duvoisin "Identification and characterization of a novel cGMP-gated channel from mouse retina."

8:15 pm Scott Nawy "Kinases and regulation of the mGluR6 cascade."

9:00 pm Laura Frishman "Response kinetics of rod bipolar cells at scotopic levels in thecat. "

15 July

Mechanisms and Functions of Gap Junctional Coupling

Moderator: Steven DeVries

9:00 am Introduction

9:10 am Doug McMahon "Structure, function and modulation of retinal gap junction channels."

9:55 am Steven Mills "Quantitative dye coupling in the retina."

10:40 am Coffee Break

11:00 am Julie Schnapf "Rod/Cone Coupling in the Macaque Retina."

11:45 am Robert Smith "Function of electrical coupling in retinal networks: adaptive filtering and noise reduction."

2:00- 4:00 PM Workshop: Optical Recording from the Retina

Moderator: Markus Meister

1) Marla Feller "Using fluorescence imaging to measure patterns of activity in the retinal ganglion cell layer."

2) Ralph Nelson "Use of voltage sensitive dyes in studies of receptor pharmacology in dissociated retinal neurons."

3) Zhuo-Hua Pan "Confocal microscopic imaging of calcium dynamics and regulation in retinal neurons."

4) David Wellis "Imaging activity along neural processes in retinal slices."

Insect Vision: Ionic Channels to Machines

Moderator: Joel Davis

7:30 pm Introduction

7:40 pm Simon Laughlin "Retinal response dynamics and visual ecology."

8:25 pm Roger Hardie "Light-sensitive channels in *Drosophila* photoreceptors."

9:10 pm Nicolas Franceschini "Understanding by reconstructing: the use of sighted robots in robotics and physiology."

16 July

Synaptic Mechanisms in the Outer Plexiform Layer

Moderator: Martin Wilson

9:00 am Introduction

9:10 am Don Dixon "Beyond synaptic excitation, metabotropic glutamate receptor actions in horizontal cells"

9:55 am Paul Witkovsky "Gain of Rod to Horizontal Cell Synaptic Transfer."

10:40 am Coffee Break

11:00 am Rukki Rao-Mirotznik "Functional architecture of the rod synapse."

11:45 am Steven Barnes "Plastic photoreceptors: Ion channel modulation."

Talks selected from poster submissions

(20 min talks, 10 min question and answer)

Moderator: Richard Masland

7:30 pm Introduction

7:40 pm Pedro de la Villa "Calcium currents in the axon terminal of mouse bipolar cells, recorded in retinal slice preparation)

8:05 pm Marla Feller "Spatial and temporal properties of spontaneous wave domains in the developing mammalian retina."

8:30 pm Rich Kramer "Cyclic nucleotide-gated channels in synaptic terminals of retinal cone photoreceptors."

8:55 pm Lei Li "Behavioral analysis of visual sensitivity in adult zebrafish."

9:20 pm Stan Schein "Cone ribbon synapses might supply basal synapses with glutamate."

17 July

GABA_C Receptors

Moderator: John Dowling

9:00 am Introduction

9:10 am Ralf Enz "Localization of the GABA_C receptor in the mammalian CNS."

9:55 am Dongxian Zhang "Mechanisms underlying the assembly of functional GABA ρ subunits in oocytes."

10:40 am Coffee Break

11:00 am Haohua Qian "GABA_C receptors in the white perch retina."

11:45 am Tian-Li Wang "GABA ρ receptor: Structure and function."

Synaptic Processes in the Inner Plexiform Layer

Moderator: Aki Kaneko

7:30 pm Introduction

7:40 pm Ruth Heidelberger "ATP and exocytosis at a ribbon synapse."

8:25 pm Martin Wilson "What is a quantum of transmitter?"

9:10 pm Peter Lukasiewicz "AMPA-type glutamate receptors may shape excitatory synaptic inputs to retinal ganglion cells."

18 July

Ecology of Vision

Moderator: Markus Meister

8:30 am Introduction

8:40 am Belinda Chang "Using comparative methods to investigate the evolution of wavelength regulation in visual pigments."

9:25 am Ed Pugh "Double-cones, double-cone mosaics and polarization-difference imaging."

10:10 am Coffee Break

10:30 am Gershon Buchsbaum "Modeling of signal sampling and propagation through multiple retinal cell layers."

11:15 am Sean McCarthy "Preferential representation of natural scenes in the salamander retina."

* Has indicated a possible conflict of interest.

Retinal Neurobiology and Visual Processing

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**FASEB
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Sutter Instrument
NSF
Avon Instruments, Inc.
U.S. Air Force
ONR**

Recent Papers of the Speakers
(Arranged in alphabetical order for each session)

Visual Performance

Banks

Allen D; Banks MS; Norcia AM . Does chromatic sensitivity develop more slowly than luminance sensitivity? Vision Research, 1993, 33:2553-62

Savage GL; Banks MS . Scotopic visual efficiency: constraints by optics, receptor properties, and rod pooling. Vision Research, 1992, 32:645-56

Banks MS; Sekuler AB; Anderson SJ . Peripheral spatial vision: limits imposed by optics, photoreceptors, and receptor pooling. Journal of the Optical Society of America a. Optics and Imagescience, 1991, 8:1775-87

Brainard

Brainard, D. H. (1995). Reconstructing images from trichromatic samples: from basic research to practical applications.. Proceedings of the IS&T/SID Color Imaging Conference: Color Science, Systems, and Applications, Scottsdale, AZ, pp. 4-10.

Williams, D. R., Sekiguchi, N., & Brainard, D. H. (1993). Color, contrast sensitivity, and the cone mosaic. PNAS USA, 90, 9770-9777.

Brainard, D. H., & Williams, D. R. (1993). Spatial reconstruction of signals from short wavelength cones. Vision Research, 33(1), 105-116.

Reuter

Copenhagen D.R., Hemilä S. and Reuter T. (1990). Signal transmission through the dark-adapted retina of the toad (*Bufo marinus*). Gain, convergence, and signal/noise. J Gen Physiol 95: 717-732.

Aho A.-C., Donner K. and Reuter T. (1993). Retinal origins of the temperature effect on absolute visual sensitivity in frogs. J Physiol 463: 501-521.

Aho A.-C., Donner K., Helenius S., Olesen Larsen L. and Reuter T. (1993). Visual performance of the toad (*Bufo bufo*) at low light levels: retinal ganglion cell responses and prey-catching accuracy. J Comp Physiol A 172: 671-682.

Leibrock C.S., Reuter T. and Lamb T.D. (1994). Dark adaptation of toad rod photoreceptors following small bleaches. Vision Research 34: 2787-2800.

Smirnakis

S.M. Smirnakis, M.J. Berry, D. K. Warland, W. Bialek, M. Meister, "Retinal Processing Adapts to Image Contrast and Spatial Scale," (manuscript submitted for publication).

S.M. Smirnakis, M.J. Berry, D. K. Warland, W. Bialek, M. Meister, "Dynamics of Adaptation to Changing Spatial Structure in the Tiger Salamander Retina." Abstract, Twenty-fifth Annual Meeting of the Society for Neuroscience, San Diego, CA, November 1995.

S. M. Smirnakis, D.K. Warland, W. Bialek, M. Meister, "Tiger Salamander Retina Adapts to Temporal Contrast Modulation to Improve Coding Efficiency." Abstract, Association of Research in Vision and Ophthalmology Conference, Fort Lauderdale, FL, May 1995

Signal Transduction and Modulation in On Bipolar Cells

Duvoisin

Duvoisin RM; Zhang C; Ramonell K . A novel metabotropic glutamate receptor expressed in the retina and olfactory bulb. *Journal of Neuroscience*, 1995 Apr, 15:3075-83.

Duvoisin RM; Zhang C; Hamassaki-Britto DE; Britto LR . Changes in expression of glutamate receptor subunits following photoreceptor degeneration in the rd mouse retina. *Neuroscience Letters*, 1995 Jan 2, 183(1-2):83-6.

Pin JP; Duvoisin R. The metabotropic glutamate receptors: structure and functions. *Neuropharmacology*, 1995 Jan, 34(1):1-26.

Britto LR; Rogers SW; Hamassaki-Britto DE; Duvoisin RM . Nicotinic acetylcholine receptors in the ground squirrel retina: localization of the beta 4 subunit by immunohistochemistry and in situ hybridization. *Visual Neuroscience*, 1994, 11:569-77

Frishman

Robson JG, Frishman, LJ. (1995) Response linearity and dynamics of the cat retina: the bipolar cell component of the dark-adapted ERG, *Vis. Neurosci.*, 12: 837-850.

Robson JG, Frishman, LJ. (1996) Photoreceptor and bipolar-cell contributions to the cat electroretinogram: a kinetic model for the early part of the flash response. *J. Opt. Soc. Am. A*, 13: 613-622.

Frishman, LJ, and Robson, JG. (1996) Inner retinal components of the scotopic ERG of the cat. *J. Brain Res.* 37: 204-205.

Frishman, LJ, Robson, JG and Viswanathan (1996) Response kinetics of retinal cells at scotopic levels in the cat. *Invest. Ophthalmol.* 37: S348.

Nawy

Nawy S; Jahr CE . cGMP-gated conductance in retinal bipolar cells is suppressed by the photoreceptor transmitter. *Neuron*, 1991 Oct, 7(4):677-83.

Nawy S; Jahr CE . Suppression by glutamate of cGMP-activated conductance in retinal bipolar cells. *Nature*, 1990 Jul 19, 346(6281):269-71.

Nawy S; Jahr CE. Time-dependent reduction of glutamate current in retinal bipolar cells. *Neuroscience Letters*, 1990 Jan 22, 108(3):279-83.

Mechanisms and Functions of Gap Junctional Coupling

McMahon

McMahon, D.G., and Brown D.R. (1994) Modulation of gap junction channel gating at zebrafish retinal electrical synapses. *J. Neurophysiol.* 72:2257-2268.

McMahon, D.G., Rischert, J. C., and Dowling, J.E. (1994) Protein content and cAMP-dependent phosphorylation of fractionated white perch retina. *Brain Res.* 659:110-116.

McMahon, D.G. (1994) Modulation of electrical synaptic transmission in zebrafish retinal horizontal cells. *J. Neurosci.* 14:1722-1734.

Mills

Mills, S.L. and Massey, S.C. (1995) Differential properties of two gap junctional pathways made by AII amacrine cells. *Nature* 77, 734-737.

Mills, S.L. and Massey, S.C. (1994) Distribution and coverage of A- and B-type horizontal cells stained with Neurobiotin in the rabbit retina. *Visual Neuroscience* 11, 549-560.

Schnapf

Schnapf, J.L., Nunn, B.J., Meister, M., & Baylor, D.A. (1990). Visual transduction in cones of the monkey *Macaca fascicularis*. *Journal of Physiology* 427, 681-713.

Kraft, T.W., Schneeweis, D.M. & Schnapf, J.L. (1993). Visual transduction in human rod photoreceptors. *Journal of Physiology* 464, 747-765.

Schneeweis, D.M. & Schnapf, J.L. (1995). Photovoltage of rods and cones in the macaque retina. *Science*, 268, 1053-1056.

Smith

Smith, R.G., and Vardi, N. (1995) Simulation of the AII amacrine cell in cat retina: Functional consequences of electrical coupling and regenerative membrane properties. *Visual Neuroscience*, 12: 851-860.

Smith, R.G. (1995) Simulation of an anatomically-defined local circuit: the cone-horizontal cell network in cat retina. *Visual Neuroscience*, 12: 545-561.

Smith, R.G. (1995) Retina. In: Michael A. Arbib (Ed.): *The Handbook of Brain Theory and Neural Networks*. Bradford Books/MIT Press.

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Insect Vision: Ionic Channels to Machines

Franceschini

Franceschini, N.; Pichon, J.M., Blanes, C. (1992) From insect vision to robot vision *Phil. Trans. Roy. Soc. B* 337, 283-294

Martin, N., Franceschini, N. (1994) Obstacle avoidance and speed control in a mobile vehicle equipped with a compound eye In: 'Intelligent Vehicles', EI. Masaki (Ed.), M.I.T. Press, Cambridge (U.S.A.), pp. 381-386

Mura, F., Franceschini, N. (1994) Visual control of altitude and speed in a flying agent In: 'From Animals to animats', D. Cliff, P. Husbands, J.A. Meyer, S.W. Wilson, M.I.T. Press, Cambridge, U.S.A, pp. 91-99

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Hardie

Hardie, R.C., and Minke, B (1993) Novel Ca^{2+} channels underlying transduction in *Drosophila* photoreceptors: implications for phosphoinositide-mediated Ca^{2+} mobilization. *Trends Neurosci.* 16:371-376.

Hardie, R.C. (1995) Caged Ca^{2+} facilitates and inactivates but does not directly excite light sensitive channels in *Drosophila* photoreceptors. *J Neurosci.* 15:889-902

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Laughlin

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Synaptic Mechanisms in the Outer Plexiform Layer

Barnes

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Dixon

Dixon, DB and Copenhagen, DR (1996) Metabotropic glutamate receptor-mediated suppression of an inward rectifier current is linked via a cGMP cascade. In preparation.

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Rao-Mirotznik

Rao, R., G. Buchsbaum, and P. Sterling. (1994) Rate of quantal transmitter release at the mammalian rod synapse. *Biophysical J.* 67:57-63.

Rao-Mirotznik, R., A. B. Harkins, G. Buchsbaum, and P. Sterling. (1995) Mammalian rod terminal: architecture of a binary synapse. *Neuron* 14:561-569.

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Witkovsky

Akopian, A. and Witkovsky, P. 1994. Modulation of transient outward potassium current by GTP, calcium and glutamate in horizontal cells of the *Xenopus* retina. *J. Neurophysiol.* 71:1661-1671

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Schmitz, Y. and Witkovsky, P. 1996. Glutamate release by *Xenopus* retinal photoreceptors: dependence on light and calcium. *J. Neurosci. Methods*, accepted for publication

GABA_A Receptors

Enz

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Qian

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Wang

T. Kusama, T-L Wang, W B Guggino, G R Cutting, and G R Uhl (1993) GABA r2 receptor pharmacological profile: GABA recognition site similarities to r1. *Eur. J Pharmacology*, 245: 83-84

T-L Wang, W B Guggino, and G R Cutting (1994) A novel g-aminobutyric acid receptor subunit (r2) cloned from human retina forms bicuculline-insensitive homooligomeric receptors in *Xenopus* oocytes. *J. Neuroscience* 14:6524-6531

T-L Wang, A Hackam, W B Guggino, and G R Cutting (1995) A single histidine residue is essential for zinc inhibition of GABA r1 receptors. *J. Neuroscience* 15:7684-7691

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Zhang

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Synaptic Processes in the Inner Plexiform Layer

Heidelberg

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Lukasiewicz

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